#### PATENT COOPERATION TREATY

# Translation

### PCT

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

| Annlinanti  |  |                   | <del></del>            |                              |                                       |  |  |  |  |
|---|--|-------------------|------------------------|------------------------------|---------------------------------------|--|--|--|--|
| Applicant's or agent's file reference P04-76  |  |                   | FOR FURTHE             | R ACTION                     | See Form PCT/IPEA/416                 |  |  |  |  |
| International application No. Ir  |  |                   | International filing   | date (day/month/year)        | Priority date (day/month/year)        |  |  |  |  |
| PCT/JP2004/010437   |  |                   | 15.07.20               |                              | 01.08.2003                            |  |  |  |  |
| Internationa  | al Patent Classificati   | ion (IPC) or nati | onal classification a  | nd IPC                       |                                       |  |  |  |  |
| C07D2   | 257/04   |                   |                        |                              |                                       |  |  |  |  |
| Applicant TOYO  | KASEI KO   | GYO COME          | PANY LIMI              | red .                        |                                       |  |  |  |  |
| <ol> <li>This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</li> </ol> |  |                   |                        |                              |                                       |  |  |  |  |
| 2. Th   | is REPORT consist  | s of a total of   | 5                      | sheets, includi              | ng this cover sheet.                  |  |  |  |  |
| 3. Th   | is report is also acc  | ompanied by AN    | NEXES, comprisin       | g:                           |                                       |  |  |  |  |
| a.  | (sent to the   | e applicant and t | o the International i  | Bureau) a total of           | sheets, as follows:                   |  |  |  |  |
|   | a. (sent to the applicant and to the International Bureau) a total of sheets, as follows:  sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions). |                   |                        |                              |                                       |  |  |  |  |
|   | sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental   |                   |                        |                              |                                       |  |  |  |  |
|   | DOX.   |                   |                        |                              |                                       |  |  |  |  |
| Ь.  | (sent to the   | International B   | ureau only) a total o  | of (indicate type and number | er of electronic carrier(s))          |  |  |  |  |
| related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).  |  |                   |                        |                              |                                       |  |  |  |  |
| 4. Thi  |  |                   | g to the following ite | ems:                         |                                       |  |  |  |  |
| $\boxtimes$   | Box No. I  | Basis of the re   |                        |                              |                                       |  |  |  |  |
|   | Box No. II   | Priority          | -                      |                              | •                                     |  |  |  |  |
|   | Box No. III  | Non-establish     | ument of opinion wit   | h regard to novelty, invent  | ive step and industrial applicability |  |  |  |  |
|   | Box No. IV   | Lack of unity     |                        |                              |                                       |  |  |  |  |
| $\boxtimes$   | Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement  |                   |                        |                              |                                       |  |  |  |  |
|   | Box No. VI   | Certain docum     |                        |                              |                                       |  |  |  |  |
|   | Box No. VII  | Certain defect    | s in the internationa  | l application                |                                       |  |  |  |  |
|   | Box No. VIII   |                   | vations on the intern  |                              |                                       |  |  |  |  |
| Date of submission of the demand  Date of completion of this report   |  |                   |                        |                              | S report                              |  |  |  |  |
|   |  |                   |                        | bate or completion of the    | steport                               |  |  |  |  |
| Tame and mailing address of the IPEA/JP   |  |                   |                        | Authorized officer           |                                       |  |  |  |  |
| racsimile No.   |  |                   |                        | Telephone No                 |                                       |  |  |  |  |

#### INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/JP2004/010437

| Box No   | o. I                                   | Basis of the report   | •   |   |
|----------|--|---|---|---|
| 1. V     | ith regard                             | d to the language, this report is based on the internati<br>nder this item.   | onal application in the language in wl  | nich it was filed, unless otherwise                                     |
|          | This i                                 | report is based on translations from the original langu<br>n is the language of a translation furnished for the pur | age into the following language poses of:                                       |   |
|          |  | international search (Rule 12.3 and 23.1(b))  |   |   |
|          | 닏                                      | publication of the international application (Rule 12.  | 4)  |   |
|          |  | international preliminary examination (Rule 55.2 and  |   |   |
| re       | ith regard<br>ceiving O<br>is report): | to the elements of the international application, this ffice in response to an invitation under Article 14 a        | s report is based on (replacement she<br>re referred to in this report as "orig | ets which have been furnished to thinally filed" and are not annexed to |
|          | the int                                | ternational application as originally filed/furnished   |   |   |
| <u> </u> | l the de                               | scription:  |   |   |
|          | pages                                  |   |   | as originally filed/furnished   |
|          | pages*                                 | ·   | received by this Authority on   |   |
|          | pages*                                 |   | received by this Authority on   |   |
| L        | the cla                                | ims:  |   |   |
|          | nos.                                   |   |   | as originally filed/furnished   |
|          | nos.*                                  |   | as amended (together wi   | th any statement) under Article 19                                      |
|          | nos.*                                  |   | received by this Authority on   |   |
|          | nos.*                                  |   | received by this Authority on   |   |
|          | the dra                                | wings:  |   | -   |
|          | sheets                                 |   |   | as originally filed/furnished   |
|          | sheets*                                |   | received by this Authority on   |   |
|          | sheets*                                |   | <u>-</u>  |   |
|          | a seque                                | nce listing and/or any related table(s) – see Suppleme  |   | <del></del>   |
| 3.       |  | nendments have resulted in the cancellation of:   | - on to-raing to boddence Distin  | ь.  |
| <i>-</i> |  |   |   |   |
|          |  | ne claims, nos.   |   | <del></del>   |
|          |  |   |   |   |
|          |  | ne drawings, sheets/figs  |   |   |
|          |  |   |   |   |
| 4.       | This rep                               | port has been established as if (some of) the amend   | nents annexed to this report and liste  | d below had not been made, since  |
|          |  | ve been considered to go beyond the disclosure as file  |   | • • •   |
|          |  | ne description, pages   |   |   |
|          |  | e claims, nos.  |   |   |
|          |  | e drawings, sheets/figs   |   |   |
|          |  | e sequence listing (specify):   |   |   |
|          |  | ny table(s) related to sequence listing (specify):  |   |   |
| * If it  | em 4 appli                             | ies, some or all of those sheets may be marked "super   | rseded."  |   |

International application No.
PCT/JP2004/010437

| Box |                                     | soned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;<br>lions and explanations supporting such statement |            |      |
|-----|-------------------------------------|---|------------|------|
| 1.  | Statement                           |   |            |      |
|     | Novelty (N)                         | Claims  | 1-11       | YES  |
|     |                                     | Claims  |            | _ мо |
|     | Inventive step (IS)                 |   | 5, 6, 8-11 | YES  |
|     |                                     | Claims  | 1-4, 7     | NO   |
|     | Industrial applicability (IA) Clair |   | 1-11       | YES  |
|     |                                     | Claims  |            | NO   |
|     |                                     | <del></del>   |            |      |

#### 2. Citations and explanations (Rule 70.7)

#### Citations

Document 1: JP 09-505275 A (Glaxo Group Ltd.), 27 May 1997

Document 2: JP 11-502810 A (Glaxo Group Ltd.), 09 March 1999

Document 3: WO 2002/006263 A1 (Chugai Pharmaceutical Co., Ltd.), 24 January 2002

Document 4: Chemical & Pharmaceutical Bulletin, 1983, Vol. 31, No. 5, pages 1751 to 1753

#### Explanations

Claims 1 to 4 and 7

The inventions set forth in claims 1 to 4 and 7 are not disclosed in any of the documents that are cited in the international search report; therefore, said inventions are novel. However, the inventions in question do not involve an inventive step in the light of documents 1 to 4 cited in the international search report.

Documents 1 and 2 disclose methods for producing compounds that are represented by general formula (2),

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Box No. V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

wherein a compound represented by general formula (1) set forth in claim 1 of the present application in which  ${\tt A}^1$ signifies a hydroxyl group is reacted with a hexamethylenetetramine in the presence of a trifluoroacetic acid, a CHO group is introduced into the benzene ring by means of hydrolysis and then the aforementioned hydroxyl group is converted into an alkoxyl group. Meanwhile, document 3 discloses a method for introducing a CHO group into a hydroxyl groupsubstituted benzene ring, wherein a given starting compound is treated by means of a hexamethylenetetramine in the presence of an acid catalyst such as a trifluoroacetic acid or a methanesulfonic acid and then the product from said treatment is hydrolysed; therein, document 3 further indicates that it is preferable to employ a methanesulfonic acid as the aforementioned acid catalyst; that it is possible to use a compound in which the hydroxyl groups are protected as the starting compound; and that the method in question is preferred because it reduces the work load. Furthermore, documents 3 and 4 both present production examples wherein a methanesulfonic acid was actually employed as the acid catalyst.

As a result, it would have been obvious to a person skilled in the art to substitute a methanesulfonic acid or other such acid catalyst for the trifluoroacetic acid, and to employ a compound in which the hydroxyl groups are protected by means of alkyl groups or the like as the starting compound in the methods for the production of compounds that are represented by general formula (2) which are disclosed in documents 1 and 2.

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Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Claims 5, 6 and 8 to 11

The inventions set forth in claims 5, 6 and 8 to 11 are novel and involve an inventive step in relation to documents 1 to 4 cited in the international search report.

The compounds that are represented by general formula (2) other than the compounds that are also represented by general formula (8) set forth in claim 7 of the present application are not disclosed in any of documents 1 to 4, and the compounds in question cannot be said to have been obvious to a person skilled in the art in the light of the disclosures in documents 1 to 4.